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PIONEERS IN NEUROLOGY

Louis Antoine Ranvier (1835-1922)

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Louis Antoine Ranvier (1835-1922)

Louis Antoine Ranvier was most prominent French histologist of the late 19th century. He held the chair of General Anatomy at the Collège de France (1875), thanks to his master Claude Bernard. Ranvier's refined histological techniques and precise observations on normal and injured nerve fibres were soon considered as classic work both in France and worldwide. Although, Ranvier was not a clinician, nor primarily interested in pathology, his "Traité technique d'histologie"[1] (1875) and observations on fibre nodes and the degeneration and regeneration of cut fibres had a great influence on Parisian neurology at the Salpêtrière.

Ranvier was born in Lyons and obtained the internat of Parisian hospitals with his friend Victor André Cornil (1837-1908). They taught private histopathology lessons in the rue Christine in Paris, which were later published as a "Manuel d'histologie pathologique"[2] (1869, 1873, 1876). Ranvier later abandoned pathological studies, when he became Bernard's assistant (1867). The discovery of fibre nodes, in the context of Bernard's physiology, led Ranvier to careful histological examinations of myelin sheaths and Schwann cells[3]. However, besides his major research interests, Ranvier occasionally collaborated with colleagues (L.T.J. Landouzy) on autopsies and histological observations of tumours and injured tissues. In 1872-1873, Ranvier combined both subjects, when he made a precise description of the degeneration of cut fibres. Ramón y Cajal later remarked on the scientific and technical contributions of Ranvier stating: "It is only the talent of such men as Waller and Ranvier that has been able to supply the

methodological deficiencies [to show the genesis, growth and evolution of the axons]"[4]

Ranvier's findings were in agreement with those of Augustus Waller (1816-1870) on the degeneration of nerve fibres separated from the centre, but refuted Vulpian's on the autogenous repair of cut peripheral fibre endings. Félix Alfred Vulpian (1826-1887), a former student of Jean-Pierre Marie Flourens (1794-1867), was an anatomopathologist, clinician and experimenter at the Salpêtrière, with the clinician Jean-Martin Charcot (1825-1893). As an experimenter, Vulpian observed the development of frog embryo's tails isolated from the body, and saw nutrition, multiplication and differentiation of cellular elements, as vital phenomena preserved in injured and isolated tissues. Thus, Vulpian thought his observations, including numerous studies on cut nerves and pathological nerve lesions, contradicted the general law promoted by Waller.

Ranvier's studies on the degeneration of nerve fibres (1872-1873)[5,6] led Vulpian to change his views after 1873, especially in the interpretation of a gain of motor function of a cut nerve, which he explained by an anastomosis with adjacent nerves. Vulpian fully admitted again Waller's law, and reproduced Ranvier's results extensively. Although Vulpian adopted most of the views of Ranvier, he persuaded his assistant Joseph Jules Déjerine (1849-1917) to re-examine the role of Schwann cell nuclear swelling in nerve fibre loss of function. In this case, Déjerine was able to refute Ranvier's hypothesis using Ranvier's own techniques. This study clearly showed the Sâlpétrière's interest in Ranvier's studies at the Collège de France.

Charcot and Vulpian's histological observations led to the description of multiple sclerosis, which they named "sclérose en plaques". This also contradicted Waller's law, since nerve fibre lesions were not associated with anterograde nerve fibre degeneration. Again, Vulpian persuaded a young assistant, Joseph Jules Babinski (1857-1932) to re-examine the problem noticed by Charcot with Ranvier's techniques, in Cornil's laboratory, after Cornil replaced Charcot at the chair of pathological anatomy at the Faculté de Médecine (1882). Babinski demonstrated multiple sclerosis could not be taken as an exception to Waller's law, because demyelination did not involve a major loss of axons' integrity.

Ranvier's observations also led Babinski to contradict Charcot's theory on the genesis of sclerosis. Charcot explained myelin loss, first demonstrated by Frommann (1864), as a passive process, with inflammatory neuroglia exerting pressure on myelin. However, Babinski noticed myelin fragmentation was similar to that observed by Ranvier in the central edge of cut fibres, and involved lymphatic cells absorbing myelin particles, as first noticed by Ranvier.

In other forms of sclerosis (sclérose systématique), Babinski noticed secondary degenerations and histological characteristics identical to those described by Ranvier, in the peripheral segment of cut fibres. Similarly, Babinski adopted unequivocally Ranvier's view on regeneration: "The sprouting of central axon-cylinders was demonstrated by Ranvier with indisputable proofs and the subject bears no discussion."[7]

Ranvier's influence on neuropathology at the Sâlpétrière is unquestionable. When Vulpian and Charcot began their anatomopathological studies (1862), histological observations on fresh and fixed tissues were rather unsophisticated. The first chair of histology in France was created for Charles Robin (1821-1885) the same year, at the Faculté de Médecine of Paris. Histology was not a technique beloved of French medical scholars, any role in the definition of pathologies was highly suspect. However, a small histological laboratory was settled in a disused kitchen at the Sâlpétrière, around 1875. Déjerine and Babinski recognised the limits of histological techniques used by Charcot and Vulpian. In this context, Ranvier's papers were highly praised, including numerous technical notes in Les Archives de Physiologie, created (1868) and edited by Brown-Séquard, Charcot, and Vulpian. His technical improvements were rapidly adopted by young histopathologists looking for novel interpretations of previously described pathologies.

However, Ranvier was first opposed to Charcot and Vulpian's schools in the study of the degeneration and regeneration of nerve fibres. Although Déjerine was always extremely respectful of Vulpian, and quoted Ranvier's work rarely, his paper refuting one of Ranvier's observations, attached great value to Ranvier's findings. Cornil, one of Charcot's first interns and Ranvier's lifelong friend, played a major role in diffusing Ranvier's techniques and probably influenced Babinski's adoption of them in his thesis on multiple sclerosis (1885).

Later, Babinski wrote in the "Traité de médecine"[8] (1894), edited by Charcot, Bouchard and Brissaud, a chapter on "Névrites", with a first part devoted to experimental nevritis, where Ranvier's observations played a major role. In this sense, Ranvier's career can be placed in the perspective of French neurology at

the Sâlpétrière. His work on injured fibres formed the basis of many subsequent observations and progress in understanding nerve fibre lesions, in diverse pathologies. While French neurology may not have shared the histological tradition developed in Germany and England, Ranvier's influence helped to make up for lost time.

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